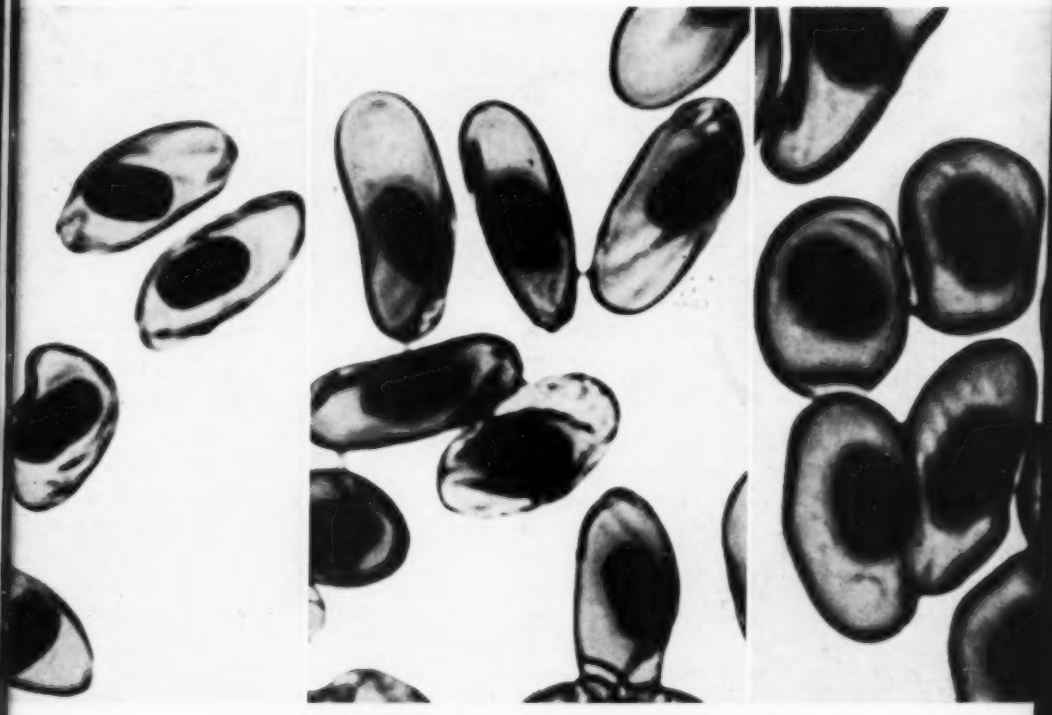
The Journal of HEREDITY



SPECIES-DIFFERENCES IN RED BLOOD CELLS
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Beginnings of Eugenical Sterilization
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Twins Test Causes of Feeblemindedness
Mutations of the Hooded Gene in the Rat
Cancer Research *vs* An Afternoon of Football
A Three-Century Human Inbreeding Experiment

VOLUME 28 NOVEMBER, 1937 NUMBER 11

The American Genetic Association

An incorporated organization devoted to promoting a knowledge of the laws of heredity and their application to the improvement of plants, animals, and human racial stocks

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The
Journal of Heredity

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COLCHICINE

The December issue will contain the first detailed illustrated account to be published of Dr. A. F. Blakeslee's discovery that by treatment with the alkaloid colchicine, plants with double or quadruple the normal chromosome number can be produced. The method has been successfully tried in over a dozen genera and seems to be of wide application. From both the theoretical and practical points of view the discovery has aroused the greatest interest. The authors discuss at length the possibilities of the method and its limitations, as far as they are now known.

A THREE GENERATION RECORD

Frontispiece

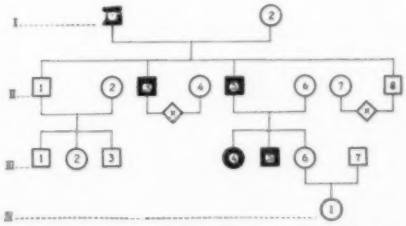
Photographs of all the dwarfs shown in the pedigree chart (Figure 1). The tallest of the dwarf members of the family scarcely exceeds a height of four feet. Musical ability was associated with dwarfism in this family, probably because the dwarfs found that their short stature enabled them to make a living most easily as performers in a band.

INHERITANCE OF NANISM IN MAN

José M. Capinpin

College of Agriculture, University of the Philippines

WHILE short stature may be considered a racial character, there are cases of extremely small stature which are clearly teratological. Just as there are dwarf varieties of plants and animals, cases of human dwarfs measuring 100 to 120 centimeters in height are known. Nanism in man is of two principal types, achondroplastic, where the limbs are short and the trunk long; and ateliotic, in which the proportions are normal but the size is reduced. Rischbeth and Barrington,[2] according to Davenport,[1] studied the heredity of these two types of nanism and concluded that abnormal heights tend to recur in families. The pedigree of a Filipino dwarf family herein described may throw additional light on the nature of inheritance of nanism.



THREE GENERATIONS OF DWARF STATURE

Figure 1

Dwarfs with bodies of normal size and short extremities are classified as achrondroplastics. In a Philippine family this form of nanism appears in three successive generations, indicating dominant mendelian inheritance. In this pedigree squares indicate males; circles, females; shaded symbols indicate dwarf individuals; diamond-X indicate childless couples.

In the pedigree chart, I-1, the progenitor of dwarf individuals had extremely short legs and arms, heavy body, and a head which is larger than the average for a Filipino. He could hardly walk, was afflicted with rheumatism most of the time and spent the day sitting at home. He earned his living by playing a mandolin, supplemented with fortune-telling by palmistry, and by acting as an herb doctor, or "herbolario." His wife, I-2, was a normal-sized woman who bore four sons, two of whom, II-1 nd II-8, were normal, and the other two, II-3 and II-5, dwarf. The oldest son, II-1, normal, married to a normal woman, II-2, had three normal children, III-1, III-2 and III-3. The second elder dwarf, II-3, married a normal woman, II-4, but had no issue. The third dwarf son, II-5, had by a normal wife, II-6, three children, III-4, a dwarf daughter who died at the age of one year; III-5, a dwarf son; and III-6, a normal daughter. The woman, III-6, a granddaugher of the dwarf male I-1, married a normal man, III-7, and gave birth to a normal daughter IV-1. The youngest son, II-8, of the dwarf progenitor, I-1, did not have any child by his normal wife, II-7.

Associated Music Ability

In this dwarf family musical ability as expressed in their accomplishments with the mandolin, was especially pronounced. It was their chief means of livelihood. It was a common experience in Los Baños to see father, I-1, and sons II-3, II-5 and II-8 form a string band (mandolin) quartet. Quite often they are hired for social gatherings. The three brothers II-3, II-5 and II-8 have already toured the Orient by serving as members of a ship's orchestra. With the exception of III-4, who died at the age of one year, all the dwarfs in this family died at mature age, the youngest one to die being 29 years old. Their heights, from grandfather to grandson, hardly exceed 120 centimeters. At the present writing the only living descendants of

this dwarf family are II-1, II-8, III-6 and IV-1.

On close examination of the pedigree chart, it will be noted that nanism or dwarfing tendency has been inherited in a direct line for three generations as a dominant trait. (See I-1, II-5, III-4 and III-5). It seems to behave as a Mendelian dominant, not necessarily sex-linked, but probably autosomal. It is not sex-limited. The evidence for the latter phenomenon is clearly shown by the dwarf daughter III-4, and dwarf son, III-5, of the dwarf father, II-5.

The nanism here described is apparently of achondroplastic type in the heredity of which skipping of a generation is known. This skipping of a generation is considered an argument against the view that achondroplastic nanism is a simple dominant trait. In the present pedigree there was no skiping of a generation, for nanism appears in three consecutive families. On the whole we may consider the conclusion of Davenport[1] to the effect that all forms of dwarfing, including ateliosis and achondroplasia, are governed by multiple dominant inhibiting factors.

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✦

ANOTHER *WHO'S WHO* TWIN

DR. R. M. HARPER reports two other twins in *Who's Who*—C. I. and Frank Millard. This brings the total score to three, which is far below the distribution of twins in the general population. When the original question of the number of twins in *Who's Who* was posed (Journal of Heredity, November, 1936), the Editor boldly took up the cudgels for twins, and held to the view that there is no reason why they should be less frequently represented in *Who's Who* than in the general population. Unless at least a dozen more pairs of twins can be assembled from that volume, the *"Who's Who* test" seems to show that Professor Harper is right, when he maintains that twins are inferior as far as their ability to gain recognition in that volume is concerned.

Professor Harper has also obtained additional data concerning the pair of twins reported at that time, which were born in different years. A later visit to Athens, Ga., confirms him in his conviction that these individuals were twins and not cousins.

"Of the Athens twins (?) above mentioned, the girl lived from November 25, 1882, to October 25, 1883, and the boy from January 23 to October 28, 1883. There was no possibility of their being cousins instead of brother and sister, for the parents were indicated in both cases. (This was verified on a visit to Athens on October 28, 1936, a little too late for inclusion in the above article.) The father lived from 1846 to 1903, and the mother from 1857 to 1923; and if they ever had any other children they may be still living, for there is no indication of them in the cemetery. (The mother's parents and a few other relatives are buried in the same lot. These grandparents both died in the same year as the twins.)

"Of course these children may not have been twins in the strictest sense, but curiously enough, two similar cases, one in the state of Washington and one in Alberta (Canada) were reported in the daily papers about the time this was published (December, 1936)."

Fertilization at different dates is not unknown among mammals, (see Journal of Heredity for April, 1932) although it is considered to be extremely rare. If twin births between which a considerable interval elapses are due to superfetation, then a question would arise whether they really are "twins" in the accepted sense of the word. "Twinning" after all has to do with multiple *birth* and how long a period can this be considered to cover?—Ed.

BREAST CANCER AND MOTHER'S MILK

Relation of Nursing to the Theory of Extra-Chromosomal Causation of Breast Cancer in Mice—A Preliminary Report

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THE existence of a carcenogenic agent in the milk which young animals obtain while they are nursing offers a possible explanation of the extra-chromosomal inheritance of breast cancer in mice. In other publications[1,2,3] it was pointed out that the incidence of breast tumors in a high tumor strain of inbred mice could be materially reduced by fostering the young of this strain as soon as possible after they were born, by females from a low tumor strain. Observations are now available on a small number of animals of the reciprocal hybrid generations between high and low breast tumor strains of mice.

Listed in the table are the data for the control (unfostered) and fostered breeding females of the "A" high breast tumor strain and the Little C_{57} Black or "B" low tumor stock. The ABF_1 hybrid generation was made by mating *A* stock females to *B* stock males. The reciprocal generation, called the BAF_1 hybrids, was derived by crossing *B* strain females to *A* strain males. The respective F_2 hybrid generations were made by crossing the F_1 mice *inter se*. The various columns in Table I show the total number of mice observed or under observation and the breast tumor incidence for the animals which have died. For comparative purposes the average breast tumor age has been tabulated for each group. The average ages of the animals dying non-tumorous (without breast tumors) and the mice still under observation are also set forth.

The breast tumor incidence for the *A* stock breeding females was 83.3 per cent (based on 788 animals), and the average tumor age was 11.5 months. Breeding females of this inbred stock which were nursed by females of the low-tumor *B* strain gave only 4.4 per cent breast tumors. The average age at death of the non-breast tumor fostered females was approximately 5 months later than that of the control group of unfostered mice (17.3 months and 12.5 months respectively).

The data published by Cloudman, Bittner and Little[4] were used for the control C_{57} Black stock group. Four females (1.0 per cent) of 386 developed breast tumors. In a group of eight *B* stock mice fostered by females of the *A* strain, three breast tumors were observed.

Ninety-one per cent of the ABF_1 (A ♀ × B ♂) have died and this group showed a breast tumor ratio of 95.8 per cent (91 of 95 mice). The average tumor age was 11.1 months and the 13 living mice average 15.7 months. Only six ABF_1 females were fostered by *B* stock mice. Two have died non-tumorous and the others are living at 14.5 months.

Ninety animals were included in the BAF_1 group of which 40 or 44.4 per cent have expired. Breast tumors developed in 12.5 per cent of this group at an average age of 13.7 months. Non-tumorous mice averaged 18.6 months at death. The living mice of the generation average 16.8 months. Thirty-five BAF_1 females were fostered by *A* stock mothers of which 15 are still living. The other 20 mice have died from breast tumors at an average age of 9.6 months.

None of the reciprocal F_2 generation mice was fostered. Sixty-seven per cent of the ABF_2 mice and 39.5 per cent of the BAF_2 mice have died and the respective breast tumor ratios were 89.2 per cent and 12.8 per cent.

Discussion

It was noted in reciprocal crosses between high and low breast tumor strains of inbred mice that the tumor incidence was markedly greater when the maternal parent was a member of the high tumor strain. To explain this phenomenon the theory of extra-chromosomal inheritance of this form of tumor was advanced by the Staff of the Jackson Laboratory in 1933.[5] Other publications supporting this theory have been made by Korteweg,[6-8] Murray and Little,[9-11] Bittner,[12-13] and Bittner and Little.[3]

In other reports on the change in the incidence of breast tumors in inbred strains following foster nursing it was suggested that the extra chromosomal or maternal influence observed in breast tumor crosses might tentatively be attributed as due to a "breast cancer-producing influence" obtained by the progeny from the milk of breast cancer line mothers.[1-3] The few additional observations make possible comparative studies in the reciprocal first generation hybrids, data from which generations resulted in the formulation of the extra chromosomal theory. At present these records are very meager but large numbers are under observation.

The percentage of the breeding females to develop mammary gland cancer in the inbred *A* and *B* stocks were 83.3 and 1.0 respectively. Following the fostering of one-day-old mice of the *A* stock by *B* stock females the incidence was reduced to 5 per cent in the first generation breeding females. The types of tumors which were observed in their progeny of subsequent generations were usually correlated with the diagnosis of the first generation mothers and has been reported. Only a few *B* females were fostered by *A* females, but the incidence of breast tumors was markedly higher than in the unfostered animals.

Reciprocal crosses were made between these two strains. When the maternal parent was from the high tumor strain the incidence of breast tumors in the breeding females of the ABF_1 generation was 95.8 per cent and in the ABF_2 generation 89.2 per cent. Corresponding ratios were 12.5 per cent in the BAF_1 generation and 12.8 per cent in the BAF_2 generation. As the average age at which the *BA* hybrid mice developed tumors was considerably less than the average age of the mice still living, the percentage of the totals in the BAF_1 and BAF_2 generations developing breast tumors will probably be less after all the animals have died.

Thirty-five BAF_1 females were nursed by *A* high tumor stock mice. Fifteen of these animals are still living but their average age is five months less than the unfostered living mice of this generation. The remaining 20 fostered BAF_1 females have developed tumors, average age 9.6 months. There is no reason to expect that this high tumor incidence will be maintained throughout the experiment. To date, however, the tumor incidence in the fostered mice of the BAF_1 generation has been 100 per cent; in the unfostered mice of the same generation it has been 12.5 per cent. Based on the total number of mice in each series, many of which are still living, the breast tumor proportion in the fostered BAF_1 females was 57.1 per cent (20 of 35) as compared with an incidence of 5.6 per cent (5 of 90) in the BAF_1 animals nursed by their *B* stock mothers.

Another series of hybrid females are under observation made by crossing females of the *B* stock to males of the *Z* or C_3H high tumor line. One group was fostered by *Z* stock females and number, the same as the unfostered class, about 40 mice. The oldest animals are eleven months. Twelve breast tumors have been recorded among the fostered breeding females and one in the unfostered group.

Further work may determine if the chromosomal constitution of the mice of the low tumor stocks must be taken into consideration as a factor effecting the breast tumor incidence following fostering by high breast tumor mice.

Only 8 *B* stock females were fostered by *A* stock mice of which three developed mammary tumors or 37.5 per cent. All of the fostered BAF_1 females which have died developed breast tumors and, including the living animals, the incidence is 57.1 per cent. These later animals obtained half of their chromosomes from the *A* stock parent and the others from the *B* stock parent.

Only six ABF_1 females were fostered by *B* stock animals. Two have died non-tumorous and the other four are living at an average age of 3.4 months greater than the average breast tumor age of the ABF_1 unfostered females. In the group of unfostered mice only four females of the 95 animals which have died were non-cancerous.

Also of interest is a small group of 14 BAF_1 females which received, when they were 6-8 weeks old, transplants of splenic tissue from ABF_1 and BAF_1 mice. The donors averaged five weeks in age. Of the five breast tumors observed in BAF_1 females to date, three have occurred in this group of 14 mice, the other two developing among the 76 mice which were not inoculated. The same is true of the BAF_2 mice. Two tumors were observed among eleven inoculated animals. The other four tumors were recorded in progeny of living BAF_1 females which were inoculated with splenic tissue or of females which were not inoculated but had developed breast tumors.

From the small number of observations on pure stock animals and their reciprocal F_1 hybrids, it seems probable that the incidence of breast tumors in mice may be increased or decreased as a result of nursing by high or low breast tumor stock females. The additional data presented here support the theory tentatively advanced previously that the extra-chromosomal or maternal influence observed in breast tumor crosses may be due to a "breast cancer-producing influence" transmitted in the milk of breast tumor stock mothers. There is some preliminary indication that this "influence" may possibly be transmitted to low tumor stock mice by the inoculation of normal tissue from potentially cancerous animals.

TABLE I. Breast tumor ratios and average ages in unfostered and fostered breeding females of the "A" and "B" (C_{57} Black) stocks and reciprocal hybrid generations.

Breeding Females	Nursed by	Total No.	No. Dead	% of Total Dead	No. of Breast Tumors	% with Breast Tumors	Aver. Age Breast Tumors	Non-breast Tumor Mice No.	Non-breast Tumor Mice Aver. Age	Living Mice No.	Living Mice Aver. Age
A	A ♀	788	788	100.0	656	83.3	11.5 Mo.	161	12.5 Mo.		
ABF_1	A ♀	108	95	90.9	91	95.8	11.1 Mo.	4	10.0 Mo.	13	15.7 Mo.
ABF_2	A ♀	97	65	67.0	58	89.2	11.5 Mo.	7	11.9 Mo.	32	15.9 Mo.
BAF_1	A ♀	35	20	57.1	20	100.0	9.6 Mo.	0		15	11.5 Mo.
B	A ♀	8	8	100.0	3	37.5	14.1 Mo.	5	18.7 Mo.		
B	B ♀	386	386	100.0	4	1.0					
A	B ♀	45	45	100.0	2	4.4	9.5 Mo.	43	17.3 Mo.		
BAF_1	B ♀	90	40	44.4	5	12.5	13.7 Mo.	35	18.6 Mo.	50	16.8 Mo.
BAF_2	B ♀	119	47	39.5	6	12.8	14.7 Mo.	41	15.9 Mo.	72	16.6 Mo.
ABF_1	B ♀	6	2	33.3	0	0.0		2	10.8 Mo.	4	14.5 Mo.

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BIOLOGICAL ABSTRACTS

Announcement of New Subscription Plan

BIOLOGICAL ABSTRACTS is a cooperative undertaking and the only instrument of its kind which abstracts and indexes the world's biological literature within the covers of a single yearly volume. This non-profit, abstracting and indexing periodical is published with the cooperation of education and research institutions, and biological journals generally, at the University of Pennsylvania, Philadelphia, Pa.

A change from an experimental to a permanent set-up for *Biological Abstracts* has been announced. The basic idea so successfully followed by the H. W. Wilson Company in publishing its periodical indexes is being adopted. Under this new plan the subscription price to institutions will be based on service rendered. It is generally agreed that educational and industrial institutions rather than individual biologists should support the abstracting and indexing of biological literature just as they now suport the indexing of the current periodical literature in other fields. The main points of the new plan include: (1) a master subscription for a given institution based on the total number of biologists on its entire staff; (2) this master subscription then entitles the institution to additional copies at $9 a volume and (3) permits personal subscriptions at $7 a volume annually. Personal and additional institutional subscriptions will not be possible unless there is first a master subscription. (4) Starting with volume 12 of the *Biological Abstracts,* abstracts will be available two or three months after the appearance of the original journals. (5) The names of the cooperating institutions as well as the journals cooperating in the abstract-to-editor-plan will be published alternately on the inside cover of the *Biological Abstracts.*

It is hoped that institutions will lend their unqualified support to this plan. Queries should be addressed to the Business Manager of *Biological Abstracts,* University of Pennsylvania, Philadelphia.

Hereditary Nature of Harelip and Cleft Palate

THE German sterilization law contains a paragraph formulated in general terms, which provides for the sterilization of persons affected with "severe hereditary bodily malformations." In the official commentary to this law the question as to whether harelip and cleft palate come under that head is answered in the affirmative. This opinion is based on far from recent researches of various authors, according to which, in certain regions of Germany with a large amount of inter-marrying and little influx of new blood, family trees are said to reveal from 20 to 25 per cent of hereditability of these two malformations. In certain small sections of the Netherlands a hereditability of 45 per cent is alleged to have been observed. It has also been noted that the families in question present other hereditary bodily infirmities.

Dr. C. H. Schröter of Münster (Westphalia) has recently published the results of his research on the subject. He studied 255 cases with respect to the ancestry of the patients and discovered likewise about 40 per cent of hereditability. The hereditarily transmissible character that produces harelip and cleft palate acts generally in a recessive manner, but in some cases there is evidence of domination. The mode of hereditary transmission is thus not fully cleared up. Schröter also found an evident correlation between the cleft formations occurring in the mouth and other bodily malformations appearing either in the same individual or in blood relatives, such as cleft tongue, polydactylism, malformation of the toes, hydrocephalus, torticollis and certain hereditary eye disorders. In keeping with the prevailing trend in Germany, Schröter recommends that all persons with harelip and/or cleft palate whose direct ancestors or blood relatives are (or have been) affected with such malformations or with any related anomalies be sterilized.—*Jour. Amer. Med. Assoc.*

COSMECOLOGY: A THEORY OF EVOLUTION

OLIVER L. REISER
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EDITOR'S NOTE: *As Professor Morgan pointed out at the last Genetics Congress, genetic advances will probably come from discoveries off the beaten path, and from the formulation of fruitful hypotheses as to how the world of the gene is put together. The main function of the* JOURNAL *is to assemble the building blocks of fact discovered by experiment and observation regarding genetic phenomena, leaving pure speculation to others. The publication of Professor Reiser's most interesting synthesis of cosmology and genetics does not signal an abandonment of this policy—only a holiday to take a brief philosophical tour of the universe!*

If, as Professor Reiser suggests, geneticists must turn to a study of the Kennelly-Heaviside layer, just after taking on X-ray physics and biological chemistry, it is a striking demonstration of how rapidly the science of heredity has developed in the last third of a century. Problems of resonance are beginning to be increasingly discussed in their bearing on the structure of matter. This brings us around to the point where students of atomic structure and of galactic structure—the infinitely small and the indefinitely large—meet on common ground. The gene seems to be located at this cosmic cross-roads.

It should be remembered, however, that mutation is not evolution, only an important tool and that conscious evolution involves a profound wisdom in its accomplishment—a wisdom which man does not always display in ordering his present affairs. Whether "radio-mutations" could build up his mind fast enough for him to keep ahead of the evolutionary parade would seem to be a serious question.

IN his interesting book, *Earth, Radio and the Stars*, Professor Harlan T. Stetson points out that the solution of the problems concerning the earth and its inhabitants in the cosmic scheme of things bids fair to introduce a new synthetic science, which he designates as *cosmecology*. The argument is that as during past generations science has passed through a highly analytic age, so in generations to come we shall pass into a synthetic age in which the results of the highly specialized fields of science will be brought together into the solution of problems which are too far-reaching to be solved by any court of specialists. Problems of the nature which Professor Stetson has in mind concern the geologist, the physicist, the meteorologist, the radio engineer, the astronomer, and even the biologist and economist. In the present paper I propose to carry still further the consideration of a problem which illustrates the kind of situation Stetson has in mind—the theory of biological evolution. I am returning to this much-discussed problem of evolution because new light from various sources indicates that Darwin's theory was incomplete, so much so that a true understanding of the evolutionary process calls for precisely the type of synthesis from all fields of science which Stetson has in mind.

As is now generally known, the four main considerations which Darwin's theory of the origin of species introduced to explain biological evolution are as follows: (1) the fact of *heredity;* (2) the doctrine of *variations,* minute and insensible, continuously appearing in offspring; (3) the idea of the *struggle for existence,* due to overpopulation in terms of available food supply; and (4) the doctrine of *survival of the fittest.* The neo-Darwinians still hold that Darwin's theory of evolution is substantially correct, and believe that the only emendations necessary lie in getting a clearer picture of the nature of the first two factors, heredity and variation. Present-day genetics is concerned principally with (1) the mechanism of heredity, about which Darwin could only speculate, since genes and chromosomes were unknown in his age; and (2) the cause or causes of

biological variations, or better, mutations, as De Vries later showed. Little progress was made in connection with the problem of the origin of biological mutations until the important work of Muller on the effect of X-rays in producing those changes which must underlie the origin of new species.

"Radio-Mutations"

In recent years a considerable number of investigations have been concerned with the possible influences of X-rays, gamma rays from radioactive substances in the earth, and the like, upon plant and animal forms subjected to irradiation by such frequencies. The fact that in experimental studies the vast majority of such induced variations is lethal does not detract from the importance of the discovery that the *rate* of biological change is greatly speeded up. Following Muller's work, it was only to be expected that the suggestion would be put forth that "cosmic rays" also play a rôle, not only in the production of new varieties of plants and animals, but possibly also in the origin of life itself and its malformations in neoplastic growths.

This new "radiational" theory of the cause of mutations is experimentally well-grounded and theoretically reasonable. Modern genetics indicates that the ultimate living units are very small; it has even been suggested that the gene is the ultimate unit of life. However that may be, these sub-microscopic units certainly determine the details of inheritance, and therefore, as R. S. Lillie has suggested, a single extreme localized oscillation of a particle within a system may form the occasion for a process involving the whole system. Thus we are brought face to face with the supposition that fluctuations in the Brownian movements in the genes may lie at the basis of mutations. Perhaps, then, radiations—possibly as little as a single quantum of energy—are sufficient to activate chemically and induce the extreme fluctuation responsible for the mutation. Such appears to be the status of the problem at the present time.

The curious thing in all this is that in the course of evolution nature apparently "loafs along" for a time and then suddenly "gets busy" and produces results. The only alternatives to explain this are (1) that the cause of mutations is some periodic (fluctuating) source of activation, or (2) that the cause is constant in amount or intensity (i.e., is non-periodic) and that some sort of relaxation-oscillation, or accumulation to a critical point, is involved. Since, however, mutations experimentally produced do not apparently show any such relaxation-oscillation effect, we return to the first possibility.

If cosmic rays are causally connected with the origin of species, there must be some periodicity in their reception (and possibly the production) of said "rays" which corresponds to the alternate periods of "rest" and "activity" in biological advance. In seeking for the cause of such periodicity it is necessary to keep in mind one other difficulty which must be met before we can claim to have a theory adequate to all the facts. The difficulty mentioned arises from the fact that the quantitative values required to produce mutants experimentally do not coincide with those of the natural radiations which are actually available at the surface of the earth. These two requirements of a cosmic ray theory of the origin of mutations, namely, of temporal periodicity and variability in amount, are lumped together because in the theory here proposed an effort is made to take care of both requirements at the same time.

The Universe-Clock

In thinking about this matter the first suggestion which is likely to occur is this: Since within the range of experiments reported during the time that physical scientists have been interested in cosmic rays (mainly since the World War) no suitable temporal periodicity in their reception has been discovered, may we not make this supposition: *Is there not some sort of periodicity in the streaming of cosmic rays to the earth, which periodicity lies OUTSIDE*

the temporal limits of recorded experiments? If so, such a cycle might be responsible for the major types of living forms and these would appear on those occasions when cosmic rays were at the flood tide. This hypothesis creates the problem of finding some cause for the supposed temporal periodicity and variability in intensity. In my first thoughts about this matter the only cyclical variation which appeared to me to possess the necessary long time-scale is the revolution of the entire Milky Way around its center. Our galaxy, a watch-like disk which carries our own earth and solar system along with it, travels at a speed of about 200 miles per second and completes a revolution every 300,000,000 years. The number of cosmic "days" necessary to complete biological evolution (up to date) would be calculated as follows: If the age of our own earth is set at 1,500,000,000 (by the radioactive clock of the geologist), the number of major "diurnal" variations of cosmic rays would be the age of the earth (one and one-half billion years) divided by three hundred million years, and the quotient thus obtained turns out to be *five.* This theory of the periodicity of the earth's reception of cosmic rays, coming from beyond or within the Milky Way and entering into the region of our solar system at certain privileged positions as our galaxy revolves around its center, turns out to be attractive when it is recalled that there are *five* major geologic areas, each correlated with the emergence of its own type of living forms. These eras and their correlative living forms are as follows: (1) the *Archeozoic*—unicellular organisms; (2) the *Proterozoic—invertebrates;* (3) the *Paleozoic*—fish; (4) the *Mesozoic*—birds, reptiles and primitive mammals; (5) the *Cenozoic*—higher mammals and primates.

There are two major difficulties with this theory in the form in which it has just been stated—aside from the considerable overlapping of the above forms of life, which is to be expected anyway. In the first place, if the periodicity in the reception of cosmic rays is correlated with the revolution of our solar system around the center of our entire galaxy, the time of each maximum increase presumably ought to be the same, when as a matter of fact the intervals between the five geologic eras are not equal and uniform; and, secondly, there is no known reason why a periodic three hundred million years "day" should make any difference in our supposed periodic reception of an extra dose of cosmic rays. Fortunately at the time the writer was developing these ideas his attention was called to an investigation by an English theorist, Dr. H. Hanshaw Thomas, on "Cosmic Rays and the Origin of Species" (*Nature,* 1936, Vol. 137, pp. 51-53 and 97-98.) This investigator points out that the ionization due to cosmic rays falls off rapidly as these rays pass through the earth's atmosphere and that if biological nuclear changes and mutations can be produced by cosmic radiation they will vary with altitude. Dr. Thomas therefore sought for a correlation between the variations of species and the intensity of cosmic rays at different heights above sea level. He finds some evidence of the origin of new species of plants at higher mountain altitudes, where the cosmic ray "showers" and "bursts" are greatest and therefore most likely to make direct hits on chromosomes. (More recently this idea was again verified through balloon tests in the stratosphere where, at a height of over 13 miles, it was shown that the mutation rate among fruit flies is accelerated to five times its pace at sea level.) The value of the suggestion of Dr. Thomas is that it lends support to the cosmic ray theory of the origin of mutations, but its defect *from our point of view* is that it does not provide for the periodicity in their reception, or the variability in intensity, which we have postulated.

In order to provide a possible explanation of this supposed periodicity let us momentarily disregard our earlier supposition about the periodicity being due either to a variable source of emis-

sion or to the rotation of our galaxy, which is supposed to bring our earth into some hypothetically privileged position with respect to some constant and possibly extra-galactic source of cosmic rays. Let us rather assume that cosmic rays stream uniformly through the earth's cosmic environment. Now we must look for some other explanation of the periodicity. The suggestion next arises that perhaps the cosmic ray showers and bursts of Dr. Thomas are raised and lowered above the surface of the earth somewhat like a stream of particles from a machine gun sweeping the horizon, except that the "horizon" of the cosmic rays is the entire earth's atmosphere. Indeed, the recent work of Carl D. Anderson and Seth H. Neddermeyer on top of Pike's Peak indicates (Cf. *Physical Review,* Aug. 1935) that cosmic rays are capable of smashing up atoms and molecules and liberating highly penetrating neutrons. Why, then, shouldn't cosmic rays, or better still the secondary radiations in the form of high-energy particles released by cosmic rays, be able to reach the genes and bring about nuclear changes in organisms no less effectively than in the hearts of atoms?

The Ion-Blanket

But what is the protective armor plate which under "normal" conditions prohibits the full measure of cosmic rays from reaching the earth and its living inhabitants? The only "blanket" which does in fact vary its height periodically is the ionosphere. It is now generally known that there is an extensive region of ionization above the earth's stratosphere. This region of ionization is irregular in height, varying from 80 kilometers to several hundred kilometers above the earth's atmosphere, though it is believed that the 100 kilometer level constitutes the region of maximum ionization. This ionosphere, the next level above the stratosphere, is frequently referred to as the Kennelly-Heaviside layer, and it is responsible for the reflection of radio waves back to the earth's surface, thus making long-distance radio transmission possible. It is known that the ionization of this layer is caused largely by the ultra-violet light from the sun and that during the day the effect of solar radiation is to increase the ionization and lower the layer, while at night there is a rise in the Kennelly-Heaviside layer.

Now we come to the next step in the development of the radiational theory of the origin of species.

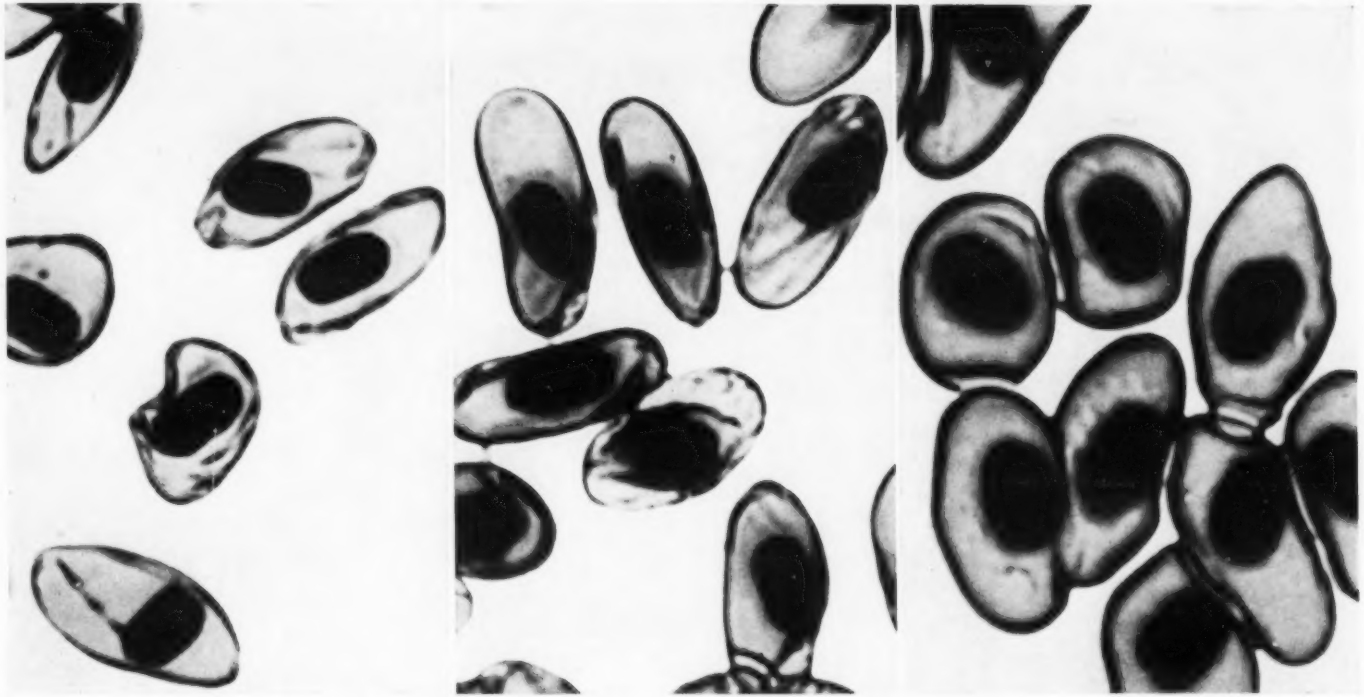
Since it is true that the highest mountains are about 800 meters high, whereas the ionosphere is about 100 kilometers high, it is necessary to suppose that some unusual source of ionization is required to bring about an effective lowering of the Kennelly-Heaviside layer, so that the cosmic rays may shower their atmospheric shrapnel over the now exposed plants and animals. The only cause for this must again be found in the sun's influence. Here we recall that while the normal ultra-violet portion of the sun's radiation is mainly responsible for the ionization, there is also an increase in ionization whenever there is an increase in sun-spot activity and a decrease whenever there is a decrease in sun-spot activity. There is no doubt but that the sun-spot cycle ionizes the terrestrial atmosphere and produces changes in the magnetic field of the earth. It is possible also that streams of particles from the sun act as ionizing agents, and thus electrons, positrons and perhaps the recently discovered neutrons, emanating from the electrically disturbed regions of the sun-spots, have their effects on the intensity of the earth's magnetism; but since ionizing agents of a corpuscular nature will be compelled to follow a curved path toward the polar regions as they approach the earth (because of the influence of the earth's magnetic field acting on such corpuscles) such particles cannot have any great effect in producing mutations in living forms around the equatorial regions, except perhaps indirectly.

On the present theory, then, we suppose that the cosmic "rays" (it does not matter whether they are photons,

uncharged electrically, or particles), which are striking the earth's atmosphere from all direction, are breaking up the neutral molecules of the gases of the atmosphere and thus helping to ionize the earth's atmosphere. But the height of the ionized layer is for the most part regulated by the mechanism of the sun, which therefore acts as a kind of pacemaker for biological evolution. With the increase in sun-spots the blanket, which normally protects life from too much irradiation by cosmic rays and ultraviolet light, is lowered to such an extent that species of plants and animals on mountain tops and lower down are showered directly with penetrating radiation and the secondary "bursts" which are produced, and thus the earth takes on the characteristics of an experimental laboratory for the production of mutations. The direct hits which reach the chromosomes induce the biological changes which are ultimately the origin of new species, and thus evolution is speeded up. Following this there must be a raising of the curtain to its former "normal" level, and organic nature loafs along again until there is a repetition of the process. It is true that this raising and lowering of the ionized layer is correlated with a decrease and an increase of atmospheric pressure (at present about 15 pounds per square inch) and this might seem incompatible with the life of land organisms, but we are dealing here with relative differences (in degree) and not with absolute changes, and the limits of variability of the earth's environment and organic adaptability may well overlap in this case.

We realize that this assumed periodic disturbance on or in the sun is still unexplained. The explanation may lie within the internal conditions of the sun, or in the wider cosmic scheme of things, or both. If the sun were a variable star, it would pulse according to its own rhythm, but it is unlikely that this rhythm would be that of the tempo of evolutionary change. It is interesting to note that Fernando Sanford, in an article on the "Influence of Planetary Configurations upon the Frequency of Visible Sun Spots" (*Smithsonian Miscellaneous Collections*, Vol. 95, 1936, No. 11), presents evidence indicating that sun-spots are related to the configuration of the planets. If this idea is verified, it follows that the dynamics of the solar system as a whole must be taken into account if we desire a complete understanding of biological evolution. And need I remind the reader that in this scheme of cosmecology we have not completely ruled out the possibility that the dynamics of the entire Milky Way, our own rotating galaxy, may still be actively involved in the process?

One interesting implication of the present theory is that evolution is not yet done with the human organism. If it is true that biologically and mentally man is still in process, and new traits yet remain to appear, one may well wonder what the future superman will be like. Interestingly enough, our own hypothesis throws some light upon the possible time of advent of a new species of humanity. Our yard-stick for measuring the tempo of evolutionary advance suggests that humanity is still in its infancy and that we will have to wait a long time before the "manhood of humanity" is reached. That is to say, the "psychozoic" age is but a small segment of the cenozoic era, which itself is relatively young. Apparently man must remain content for a long time to come before any radically new changes take place—unless, through radio-eugenics, we take the fate of biological evolution into our own hands, and in that event we may find it feasible to create or remake human nature to suit the requirements of our social architects. Adrian, the distinguished physiologist, holds that man's social progress had reached a point where he needs a larger brain to guide him in an increasingly complex world. If this view is correct, the induction of mutations, and their selective utilization may offer our one true hope for a genuinely creative control of conscious evolution.



SPECIES DIFFERENCES IN RED BLOOD CORPUSCLES

Figure 2

Red blood corpuscles (erythrocytes) of two sub-species of salamanders, *Triturus viridescens viridescens* (left), *T. viridescens symmetrica* (center) compared with a distinct species, *T. pyrrhogaster* (right). The forms which on taxonomic grounds are held to be closely related, prove with respect to blood size also to be more alike than their Japanese cousin.

BLOOD MAY TELL

Popular Adage Confirmed in Study of Blood-cell Size in Salamander Species

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THE common tieup in non-technical terminology between blood and genetic attributes has, at least in reverse English, found some justification in the present study.

Triturus viridescens viridescens and *T. viridescens symmetrica* are regarded, according to the usual taxonomic criteria, as races of the same species. *T. pyrrhogaster,* the Japanese form, however, is of a different species. This present study which has been confined to the comparative size of erythrocytes of these animals has possibly provided an additional index to their genetic relationship.

Measurements of camera lucida drawings of the red-blood cells of the three species, enlarged to the same magnification, show that in *viridescens symmetrica* the smallest cells were 1.6 square centimeters in area while the largest were 3.0 square centimeters. The average for total cell size was established at 2.3 square centimeters. Nuclear sizes in this group varied from 0.3 square centimeters to 1.2 square centimeters with the average established at 0.9 square centimeters.

The cell and nuclear areas of *T. viridescens viridescens* were larger than those of *T. viridescens symmetrica* but much smaller than those of *T. pyrrhogaster.* The average cell size for *T. viridescens viridescens* was found to be 2.56 square centimeters while the average nuclear size was 0.96 square centimeters. The range for cell size was 1.4 square centimeters to 3.7 square centimeters and that for nuclear size was 0.3 square centimeters to 1.9 square centimeters.

The erythrocytes of *T. pyrrhogaster* were found to be much larger than those of either *T. viridescens viridescens* or *T. viridescens symmetrica.* The smallest cell measured 1.9 square centimeters in area while the largest measured 6.0 square centimeters. The average for this species was 3.8 square centimeters for total cell area. The nuclear sizes of this form varied from 0.5 to 2.0 square centimeters, the average being 1.2 square centimeters.

Age Differences

The individual differences occurring in cell size in any one animal is most probably due to the difference in age. Jordan 1932[1] has shown that senile types of erythrocytes within a given individual are larger than newly formed ones. However, the marked difference in cell size occurring in *T. pyrrhogaster* as contrasted with those of *viridescens* or *symmetrica* may very well mean that there is no close genetic relationship. On the other hand such small differences in total erythrocyte size between *viridescens* and *symmetrica* on this basis would seem to indicate a much closer kinship.

These data suggest a correlation between gross external taxonomic detail, which has previously been established, and at least certain internal microscopic structures in the forms studied.

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* The above observations were part of a thesis presented in partial fulfillment of the requirements of the degree of Master of Science, August, 1937. The author acknowledges the help and advice of Professor Robert T. Hance, University of Pittsburgh, in carrying on his investigations.

BEGINNINGS OF STERILIZATION IN AMERICA

An interview with Dr. Harry C. Sharp, who performed the first operation nearly forty years ago

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ALTHOUGH the history of sterilization for eugenic purposes covers a period of 39 years in the United States, few people know that the man who began this practice, Dr. Harry C. Sharp, is still active in the medical profession. An account of the early history of sterilization was given recently in this JOURNAL[2]. Today the operation pioneered by Dr. Sharp is used with slight modification in all sterilization operations on males. First legalized in 1907 by the Indiana Legislature, sterilization now is sanctioned in 28 states and in several foreign countries—notably Germany.[5]

In order to get on record some of the details, I recently visited Dr. Sharp, who is now attached to the Veterans Hospital, Lyons, New Jersey.

During the late '90's, the operation of vasectomy began to be widely used by genito-urinary surgeons, mainly in connection with prostate operations. Dr. A. J. Ochsner, of Chicago, one of the leading surgeons of his generation, performed two such operations in 1897, and reported them in the *Journal of the American Medical Association*, April 22, 1899.[1] Both operations were entirely successful, and his patients stated that no change whatever had been noted in their sex lives. This led Dr. Ochsner to consider the eugenic application of vasectomy. He gave to his paper the title, *Surgical Treatment of Habitual Criminals*, and concluded it by saying:

> This method would protect the community at large without harming the criminal. The same treatment could reasonably be suggested for chronic inebriates, imbeciles, perverts, and paupers.

He was at that time physician at the penal institution in Jeffersonville, Indiana, Dr. Sharp related, as we sat together at the Hospital, on that beautiful Columbus Day, in Norhern New Jersey. Continuing he gave this account of the first case of eugenical sterilization:

> We had an inmate, a boy from Missouri, who complained of excessive masturbation, and insisted upon castration. I did not feel justified in performing that mutilation, and explained to this fellow, Clawson, that I could perform another operation, vasectomy, which had all the effects of castration, so far as getting him away from masturbation was concerned. Perhaps I misrepresented the facts to him; but we did not know so much about sexual science in those days.
>
> I convinced the patient that he would receive all the benefits that should be expected, and performed the operation, on October 12, 1899, exactly thirty-five years ago today. Several weeks afterwards, he reported that he was still masturbating and saw no change in his feelings. At my request, he brought a sample of his ejaculation, which was found under the microscope to be sterile. I gave him another "treatment" and told him to wait for six months; then, if he still desired it, I should castrate him.
>
> He reported later that he had stopped masturbating; felt very little desire to do so; his mind was better, and he was making better progress in school. (We were conducting a little elementary school in the institution.)
>
> Here was an operation that would not mutilate the patient, nor impair his health, and yet, would apparently improve the nervous system. Other inmates began to request that they have the advantage of the same operation.

First Accounts

Dr. Sharp read his first paper on the subject at the Mississippi Valley Medi-

cal Association meeting at Put-In-Bay, in the Fall of 1901. In the Winter of 1902, he published in the *New York Medical Journal* an article of fundamental and historic importance, entitled, *The Severing of the Vasa Deferentia, and its Relation to the Neuropsychopathic Constitution.*[3]

In this, he cited Dr. Ochsner's paper, above-mentioned, and an address by Dr. Daniel Brower of Chicago (Medical Aspects of Crime), before the American Medical Association in 1899, which also recommended vasectomy for eugenical purposes. It is very interesting to note that the early use of this measure was on criminals, rather than on the insane and feeble-minded. Since then, the tendency has been to apply it to the two classes just mentioned, but rarely to criminals as such.

Up to the time of writing of this article, Dr. Sharp wrote, he had personally vasectomized forty-two patients, who ranged in age from seventeen to twenty-five. He first followed the method which Dr. Ochsner had described, making an incision over the inguinal ring.

> Latterly (he continued) I have been following the English method, which selects the scrotal region as the site of the operation. They clasp the vas between thumb and index finger, making a longitudinal incision about three-eighths of an inch in length, and sever the vas; thus ending the operation, as they do not close the scrotal wound.

This is approximately the technique used at the present time. Recalling his early experiences with vasectomy, Dr. Sharp went on to say:

> Operations at Jeffersonville were performed on the personal request of the individual, with written consent, prior to the law of 1907. All patients were called in from six months to a year later, to report on their condition.
>
> When the Sterilization Bill was introduced in the Legislature in 1907, I had all the men sit down in their cells and write a record of their experiences, in the form of testimonials, to impress upon the legislators that there was no kick from, and no subjection of the individual to "cruel" and "unusual punishment."
>
> After the bill was adopted, the late Governor, Thomas R. Marshall, insisted that it be repealed. I had a conference with him and persuaded him not to have the Legislature repeal the Act, with the assurance that so long as he was governor, the institution would not carry out the law by performing operations.
>
> However, in 1910, there was an International Conference, under the auspices of the American Prison Association, and there was in attendance a doctor from Russia, an official delegate, who had been instructed by his government, in attending this meeting, that he must report that he had personally witnessed a sterilization operation. I made a private appeal to Governor Marshall, to let me demonstrate the operation for this Russian doctor, provided an inmate consented, which he did.
>
> Previous to the passage of the law, all patients gave their consent in writing, but, after the passage of the law, consent was no longer needed.

In June, 1909, Dr. Sharp read a paper on the subject[4] in the Section of Preventive Medicine and Public Health of the American Medical Association, meeting at Atlantic City, giving an outline of his views on eugenics, which sound very modern, even twenty-eight years later. He noted, for instance, that defectives usually mate with *their own kind*. He pointed out that an individual defective may be useful to the community, yet his posterity may be quite the reverse. He discussed various measures taken (marriage laws, segregation) to curb the multiplication of the unfit, and showed their limitations.

Referring to vasectomy, he there remarked:

> I have been doing this operation for over nine years. Four hundred fifty-six cases have afforded fine opportunity for post-operative observation, and I have never seen an unfavorable symptom.
>
> And this is the point in which this method of preventing procreation is so infinitely superior to all others proposed—that it is endorsed by the persons subjected to it.

In the following discussion, Dr. Sharp's comment showed that voluntary sterilization among professional men was already under way. "I began this work in October, 1899," he said, "and from 1899 to 1907 this operation was done on one hundred seventy-six men in the Indiana Reformatory, on request. I have operated on three phy-

sicians, and they have all assured me that they have a decided lessening of muscular and nervous fatigue."

Unfortunately, all of Dr. Sharp's early records at the Indiana Reformatory were lost in a fire, so the full details of this early history can never be regained.

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LIGHT IN THE DARKNESS

RECENTLY we have had in the Journal a spell of inky noses having their origin in the complicated subject of cancer research and its unsatisfactory and incomplete status at the moment. The editor was accused of overstepping editorial proprieties in criticising an attempted summary of the state of cancer research. It is a pleasure, therefore, to call attention to a booklet, which in its entirety occupies less space than the chapter previously criticized, and which, while making no claim to cover the whole field, nevertheless does manage to do an excellent job covering much of it, and in the process gives the lay reader an excellent idea of what is doing in this important field of inquiry.

This publication is of added interest because it represents a method of presentation of scientific research to the lay reader in rather striking contrast to that criticized earlier. Science has advanced to the point where, as was admitted by all parties in the recent discussion, "no one man can be proficient in any except a small branch of any given subject." The non-technical writer on science on a broad front is almost inevitably attempting to produce near-miracles of summary and interpretation almost from the start. This publication*, authored anonymously "by the Editors of *Fortune*", represents not an individual reaction to a research "front," but a cooperatively compiled and critically evaluated group synthesis. Thus by its very method of approach there is some likelihood that the inevitable "lack of proficiency" of even a gifted lay writer is balanced by the reactions of other critics who are covering the same ground. The resulting synthesis may not sparkle as brilliantly as an individually compounded "piece", but it has a definite lustre, and it gives a satisfactory and well rounded picture. The contrast between the two books may, therefore, represent a most interesting contrast of methods of approach to the perplexing problem of lay enlightenment regarding scientific progress.

Be that as it may "The Great Darkness which engulfs 135,000 lives per year, and which only a new light from the scientific laboratories could dispel entirely" gives the high lights of our knowledge and our ignorance regarding cancer with commendable accuracy and restraint. The specialist in genetics may feel that not quite enough significance has been attributed to family history studies and that the progress made in producing strains of mice showing definite incidences of particular forms of cancer is somewhat underrated. Doubtless those on the firing line on other research fronts might feel somewhat the same way, but all of them must admit and ad-

*The Great Darkness, Cancer. By the Editors of "Fortune". Pp. 80. Price, $1.00. New York: Doubleday, Doran & Company, Inc. 1937.

mire the fair-minded, straightforward presentation of the facts (and the courageous attempt to list the more serious lack of facts) which we have concerning this greatest cause of death among people over 45.

As a sample of the type of analysis presented, we can do no better than to quote the paragraphs dealing with the present situation with regard to the extent and the financial support available to cancer research in this country:

Only one element in the entire situation tends to allay rather than to arouse fear. This is the loosely held belief that a tremendous effort is being made to solve the cancer problem. If the doctors are making all this effort, what can the layman contribute? It is part of wisdom to hope and wait, cheered on by the thought that thousands of trained minds are attacking the subject, supported by endowments commensurate with the importance of the disease.

Unhappily, such is not the case. Hundreds of highly trained specialists supported by millions of annual dollars are at work upon cancer. But of these the vast majority are busy at the clinical end, devising emergency measures to save or prolong the lives of those who already have cancer. The amount of money provided for the search for cancer *causes* is dramatically small. There are not over two dozen funds in the United States devoted to fundamental cancer research. They range in capital from $500 up to about $2,000,000, but their aggregate capitalization is certainly not much more than $5,000,000. Their aggregate income from investments might be something like $200,000, their aggregate income from contributions some $250,000. Add another $250,000 (as a pure guess) to represent more or less direct expenditures in the cancer cause by all the universities in the land, and you have a total of $700,000 as the sum spent on cancer research in the United States each year. The public willingly spends a third of that sum in an afternoon to watch a major football game. Even so, if the $700,000 income were concentrated in one or even a few laboratories, it would be substantial. But since it is scattered throughout the forty-eight states, much of the work done with it is repetitive, some of it elementary, not a little of it wasted.

In the entire cancer field there are only two funds whose capitalizations are in excess of $1,000,000. The biggest is the International Cancer Research Foundation founded in Philadelphia in 1932 by William H. Donner with a capital of $3,000,000, which that shrewd ex-steel master (Donner Steel, Republic Steel) has ably administered ever since. Headed by Mr. Donner, an advisory committee of scientists, and a Board of Trustees, the foundation's income is parceled out to a number of cancer-research projects in various parts of the world. The next-biggest fund is that of the Crocker Cancer Research Fund in New York, created by the will of George Crocker in 1911 with a capital of $1,400,000, and headed by the distinguished cancer authority, Dr. Francis Carter Wood. The income from this fund goes entirely to Columbia University's Institute of Cancer Research, which is therefore the most heavily endowed cancer research organization in the United States. Smaller funds are the $650,000 Anna Fuller Fund of New Haven; the $400,000 Jonathan Bowman Fund at the University of Wisconsin; the $200,000 Henry Rutherford Fund at the Rockefeller Institute, which aids the institute's Division of Cancer Research, headed by Dr. James B. Murphy; the $100,000 C. P. Huntington Fund, which goes to New York's Memorial Hospital, headed by the renowned Dr. James Ewing (but of $500,000 spent on cancer by this institution in 1936, only $50,000 went to research); the $100,000 Bondy Fund at Columbia University; the $100,000 Charles F. Spang Foundation, whose income goes to the University of Pittsburgh's medical school; and the $100,000 Mack Memorial Foundation, which is partly for cancer research and goes entirely to the University of California. All other funds in the field are less than $100,000. A vital unit in the research field is Dr. Clarence Cook Little's laboratory in Bar Harbor, Maine (the Roscoe B. Jackson Memorial Laboratory), which has virtually no working capital at all save that which Dr. Little raises by personal efforts. Dr. Little breeds pedigreed mice and sells about 50,000 of them a year to cancer researchers.

The most generous contributor to the cause of cancer research is the United States Government. The United States gave only $34,000 in 1930, but the amount has been stepped up to $100,000 in 1936 and will be $140,000 in 1937. The average for the eight years 1930-37 inclusive was almost $95,000. These sums stand out as among the biggest in the field, the investment income of the International Cancer Research Foundation (Donner) being well under $100,000 and that of the Institute of Cancer Research (Crocker) only $67,000. By contrast, however, the Department of Agriculture spent $846,500 on "all phases" of cotton research in fiscal year 1936, $507,000 for "utilization of forest products," $367,000 for dairy-cattle research.

Moreover, owing to the complexity of cancer research and the fact that no one knows from what department of human knowledge the eventual solution may come, an apparent confusion confronts any young man as he approaches this field. There is only one chair of oncology (the study of tumors) in the entire United States, this being held at Cornell's Medical College by Memorial Hospital's Dr. James Ewing. At Yale the cancer research is coordinated under Dr. George M. Smith, but it is actually carried on in many different de-

partments, including anatomy, chemistry, genetics, and pathology. At Harvard there are three groups—the Harvard Medical School, whose cancer-research investigations receive yearly grants from the United States Public Health Service ($50,000 in 1935); the Department of Chemistry, which contributes the distinguished Louis F. Fieser; and the Collis P. Huntington Memorial Hospital, headed by Dr. Joseph C. Aub, physiologist, and William Salter, enzyme chemist. The three cooperate but are not closely integrated. Nowhere in the United States is there a big cancer institution with ample funds.

The "value" of research is a delicate matter to determine, as are so many other things. That we should have television, and better roads, and long staple cotton free from boll weevils is altogether admirable. The failure of radios to sprout pictures or of detours to vanish utterly is only an irritation; it does not involve the death in agony every year of enough of our friends and neighbors (speaking of the people of the United States as a whole) to populate a city larger than Wilmington, Delaware, or Ottawa, the capital of the Dominion of Canada. This is due to the darkness of ignorance which research can certainly palliate and may cure altogether. Is this tragic Darkness to continue because the light of knowledge may cost as much as a dozen, a hundred, or a thousand football games?

Since the publication of *The Great Darkness* there is increasing hope that the disparity between the funds available for football and for cancer research will be somewhat lessened. Yale University has announced an endowment of approximately ten million dollars to be used primarily for the latter purpose. The recent unanimous passage by Congress of a bill to appropriate $700,000 to be spent, under the direction of the Surgeon General and an advisory committee, on research in cancer is encouraging and represents, it is hoped, the first of a long series of annual appropriations for at least that amount.—R. C.

CAUSES OF MENTAL DEFICIENCY

IN this monograph are included the case histories of 366 pairs of twins, in which one or both members of each pair are mentally deficient. Of these, 126 pairs are presumably monozygotic, 101 pairs like-sexed dizygotic, and 139 pairs opposite-sexed dizygotic. An I.Q. of 79 is considered the upper limit of mental deficiency, and pairs showing 5 points or less difference in I.Q. are considered to be affected similarly. In 8.7 per cent of the monozygotic twins only one member of the pair is affected, whereas such complete discordance is found in 38.6 per cent of like-sexed dizygotic, and 52.5 per cent of opposite-sexed twins.

In opposite-sexed twins, the percentage of affected males was found to be 27 per cent greater than that of females. Data from Goddard's published pedigrees of mental deficiency and from 308 pairs of twins and 880 groups of siblings of normal or superior intelligence are also cited.

The authors interpret their data as indicating that hereditary factors determine "merely the potentially maximal intellectual development that may be attained by a given individual. In order that this potentiality may be fully realized favorable conditions must prevail through the various developmental periods." They further state that "it would seem that scarcely more than one-half of the cases of mental deficiency are of hereditary origin." They find that hereditary factors are more evident in cases free from such complications as infantile paralysis and epilepsy, and that

*Psychological Monographs 216. The Etiology of Mental Deficiency with Special Reference to Its Occurrence in Twins: A Chapter in the Genetic History of Human Intelligence, A. J. Rosanoff, L. M. Handy, and I. R. Plesset. Pp. 137, $2.00. Psychological Review Company, Princeton, New Jersey.

they are also more important in the higher than in the lower grades of mental deficiency. Evidence is given that about one-fifth to one-fourth of the difference between the sexes in the occurrence of mental deficiency is attributable to sex-linked genetic factors. They believe that the remainder of the difference between the two sexes "is attributable to the relatively greater vulnerability of male fetuses which renders males more liable to develop relative or absolute mental deficiency as a result of cerebral birth trauma." They present evidences not only from their own findings, but from other sources as well, indicating cerebral birth trauma to be a highly important factor in the etiology of mental deficiency.

Some of the assumptions upon which the authors base their conclusions are highly questionable. For example, one of the criteria used for attributing a trait solely to heredity is that "if found in one of a pair of dizygotic twins, it is commonly absent in the other." Evidently the authors forget that dizygotic twins are as similar in hereditary make-up as brothers and sisters. Taken as a whole, however, the data are carefully analyzed and the conclusions deserve serious consideration. The authors do not offer their conclusions as being fully proven, but rather as suggestions meriting further investigation.

The volume is a valuable source of material for anyone interested in feeblemindedness and its causes.

D. C. Rife

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A JAPANESE HUMAN INBREEDING "EXPERIMENT"

Fate and Custom Set Stage for Development of a Community Closed to Outside Blood for Over Three Centuries

On the coast of western Japan called Oita there is a small fishing village known as Usuki, where the inhabitants have strictly kept the custom of intermarriage for hundreds of years and are said never to have married the people of other villages in the neighborhood. Dr. Takeshi Ikemi, who has been investigating the biologic influence of intermarriage in the village since 1933, reports that, according to tradition, this village was settled in 1605. The villagers still believe that they are the descendants of a noble family which was obliged to flee in the civil war of the sixteenth century. There are 135 families having 1,786 members in all (904 men and 882 women). They have never mingled with other villagers or townsmen except in business transactions; consequently their habits and customs are quite different from other Japanese. The ceremonies of coming of age, marriage, burial, ancestral worship, and bringing up children are all held in their own way within their own village, and they strictly refuse to be assimilated. They are somewhat ferocious and sly, but sometimes are quite candid. The men engage in fishing and a little farming, while the women deal in the fish which the men collect and dry. They have no religious faith in its true sense, and they think little of schooling, partly because they are too poor to send their children to school. Although the children are not regular attendants at school, an investigation of the school records shows that they generally do well at school. Thus intermarriage never affected their intellectual faculties. Crime is rare. During the last ten years seven violated the fishing law, four injured others, four did some stealing, four broke the law of weights and measures, eight were charged with gambling, one cheated others, two were robbers, five interfered with government officials in the execution of their duty, and three other derelictions brought the total instances of malfeasance to thirty-eight. Judging from this, it may be affirmed that intermarriage does not bring about the degeneration of mental control. This number of violations is small when compared with that of the neighboring villages or towns.

The sanitary knowledge of the people is meager; they have epidemic diseases, such as dysentery and cholera, but there is never any serious hereditary disease. Leprosy, syphilis and elephantiasis at present are not seen among them. Neither color blindness nor insanity occurs. The constitution of the people is strong and they are good wrestlers in spite of their taking very simple food. In the physical examination for conscription, these villagers have always ranked first, in that perfecture, with respect to health and constitution. In their daily life the men are quiet and amiable, while the women are talkative. When a quarrel does occur the women are usually the leaders. However, they are usually kind and good to one another, especially to those in dis-

tress. Divorce is rare. [Detailed figures of births and deaths in Usuki village and in two neighboring villages show that intermarriage has not reduced fertility or increased mortality.—Ed.

There are now twenty-seven couples who married cousins. Through various inquiries, the following facts have been obtained: When the parents are both excellent mentally and physically, 80 per cent of the children are as excellent as their parents, 20 per cent are good, and none are worse than the parents. If the parents are good though not excellent, 15 per cent of the children are excellent, 75 per cent are as good as their parents and 10 per cent are not as good as the parents. On the contrary, if neither of the parents is good, the children are all inferior to the children of other families at large. If the parents are both good physically but not mentally, the children are all good physically, 10 per cent of them are excellent mentally, 70 per cent are mentally good and 20 per cent are inferior. To sum up, when the excellent are married, no bad results are to be found.—*Jol. Amer. Med. Assoc.*, Jan. 23, 1937.

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Dangers of Cousin Marriages

In a letter to the medical journals, Prof. J. B. S. Haldane states that the Committee on Human Genetics, appointed by the Medical Research Council, has obtained the cooperation of hospitals in an extensive inquiry on the question of the danger of marriages between cousins. All patients in the participating hospitals are being asked whether their parents were related and if so how. The preliminary results are encouraging. Certain rare conditions seem to be rather commoner among the progeny of related than among those of unrelated parents. But the results will not be statistically significant until at least three times the present number of cards have been completed. More data are particularly desired from country districts, where more inbreeding occurs than in towns.

There has long been the belief that human inbreeding is undesirable and some unions of blood relations are forbidden by law. Professor Haldane points out that recent research has shown that certain diseases are much more common among the offspring of blood relations than in the general population. The following percentages of marriages between first cousins have been found among the parents of patients suffering from the following diseases: xeroderma pigmentosum, 47; retinitis pigmentosa, 27; juvenile amaurotic idiocy, 15; ichthyosis congenita, 14. But researches into rare diseases gives little idea of the importance of the phenomenon for general health. The fact that the children of first cousins are some thirty times more likely to develop retinitis pigmentosa than the general population does not show whether such abnormalities (due to rare autosomal recessive gene substitution) are sufficiently common to render the marriage of cousins undesirable. Animal experiments give no clear answer. In some species the inbreeding of members of wild populations leads to numerous recessive abnormalities; in others it does not. Hence the need for the present investigation.—*Jour. A. M. A.*, April 25, 1936.

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Books Received

BOOKS are acknowledged in this column as received, and such acknowledgment must be regarded as sufficient return for the courtesy of the sender. As far as space permits, books that contain material of special interest to the readers of the JOURNAL *will be reviewed in later numbers.*

THE CHEMISTRY OF NATURAL PRODUCTS RELATED TO PHENANTHRENE, *by* L. F. Fieser, Associate Professor of Chemistry, Harvard University. Second Edition, With an Appendix. Pp. 456. Price, $7.00. New York: Reinhold Publishing Corp. 1937.

RASSE UND KRANKHEIT, Herausgegeben von Dr. med. Johs. Schottky. Pp. 468. Price, Mk. 21.60. Munchen 2, S. W., J. F. Lehmann's Verlag. 1937.

THE LIVING WORLD, *by* Samuel H. Williams, Professor of Zoology in the University of Pittsburgh and Associate Director of the University Lake Laboratory. Pp. 704. Price, $3.60. New York: The Macmillan Co. 1937.

VITAMINS IN THEORY AND PRACTICE, *by* Leslis J. Harris, Sc.D., D.Sc., Nutritional Laboratory, University of Cambridge, and Medical Research Council. Pp. 242. Price, $3.00. (Sec. Ed.). Cambridge: The University Press, and New York: The Macmillan Co. 1937.

COLLOID CHEMISTRY—PRINCIPLES AND APPLICATIONS, *by* JEROME ALEXANDER. 4th Ed. Pp. xvii + 505. Price, $4.50. New York: D. Van Nostrand Co. 1937.

VERERBUNG UND ENTWICKLUNG, VON HERMANN MUCKERMANN. Pp. 213. Price, M 4.40. Berlin und Bonn: Ferd. Dummlers Verlag. 1937.

HEMOPHILIA, Clinical and Genetic Aspects. Illinois Medical and Dental Monographs, Vol. I, No. 4, *by* CARROLL LAFLEUR BIRCH, M. D., Assistant Professor of Medicine. Pp. 151. Price, $2.50. Urbana, Illinois: University of Illinois Press. 1937.

DARWIN'S THEORY APPLIED TO MANKIND, *by* ALFRED MACHIN, with a Foreword by Sir Arthur Keith, F.R.S. Pp. 284. Price, $3.00. London, New York, Toronto: Longmans, Green and Co. 1937.

RACE, A Study in Modern Superstition, *by* JACQUES BARZUN. Pp. 353. Price, $2.50. New York: Harcourt, Brace and Company. 1937.

When we get ourselves talked out of the idea that human beings differ from one another in any respect, we can start proving there are no differences between species, genera, orders, etc. In the end it may turn out that we are all amoebae after all, and that all the rest is "superstition." Granting there has been a lot of foolish stuff written about race, isn't there just a modicum of actuality in the concept? Mr. Barzun thinks not.

BIOLOGICAL TIME, *by* P. LECOMTE DU NOUY, Chief of Division of Molecular Biophysics, Pasteur Institute, Paris; formerly Associate Member of the Rockefeller Institute. With Foreword by Alexis Carrel, M. D. Pp. 180. Price, $2.00. New York: The Macmillan Co. 1937.

A relativity of living processes.

SPONTANE UND STRAHLENINDUZIERTE MUTABILITAT, VON H. STUBBE, Kaiser Wilhelm-Institut für Biologie, Berlin-Dahlem. Price, M. 6.80. Pp. 190. Leipzig: Georg Thieme. 1937.

NATURAL LAW IN THE ECONOMIC WORLD, *by* WILLIAM WILCOX GREEN, B. S. Pages 151. Price, $1.50. Boston: The Christopher Publishing House. 1937.

Adam [Smith] had it — the profit motive cannonized.

EXPERIMENTELLE MUTATIONSFORSCHUNG IN DER VERERBUNGSLEHRE Beeinglussung der Erbanlagen Durch Strahlung und Andere Faktoren, *by* N. W. TIMOFEEFF-RESSOVSKY. Pp. 183. Price, RM 16.50. Dresden und Leipzig: Verlag von Theodor Steinkopff. 1937.

A HANDBOOK OF STATISTICS FOR USE IN PLANT BREEDING AND AGRICULTURAL PROBLEMS, *by* F. J. F. SHAW, C. I. E., D. Sc., A. R. C. S., F. L. S., Imperial Economic Botanist and Director, Imperial Institute of Agricultural Research, Pusa. Pp. 182. Price, Rs. 4-6 or 7s. 3d. Delhi, India, Manager of publications, Imperial Council of Agricultural Research. 1936.

SAFELY THROUGH CHILDBIRTH, A Guide Book for the Expectant Mother. Pp. 192. Price, $2.00. CHILDBIRTH: YESTERDAY AND TODAY, The Story of Childbirth Through the Ages, To the Present. Pp. 192. Price, $2.00. *By* A. J. RONGY, M. D. New York: Emerson Books, Inc. 1937.

AMERICAN WOMEN, The Official *Who's Who* among the Women of the Nation. Volume II, 1937-1938. Pp. 826. Price, $10,00. Durward Howes, Editor. Los Angeles: American Publications, Inc. 1937.

THE LITTLE THINGS IN LIFE, The Vitamins, Hormones, and other Minute Essentials for Health, *by* BARNETT SURE, PHD. Professor of Agricultural Chemistry in the University of Arkansas. Pp. 340. Price, $2.50. New York: D. Appleton-Century Co. 1937.

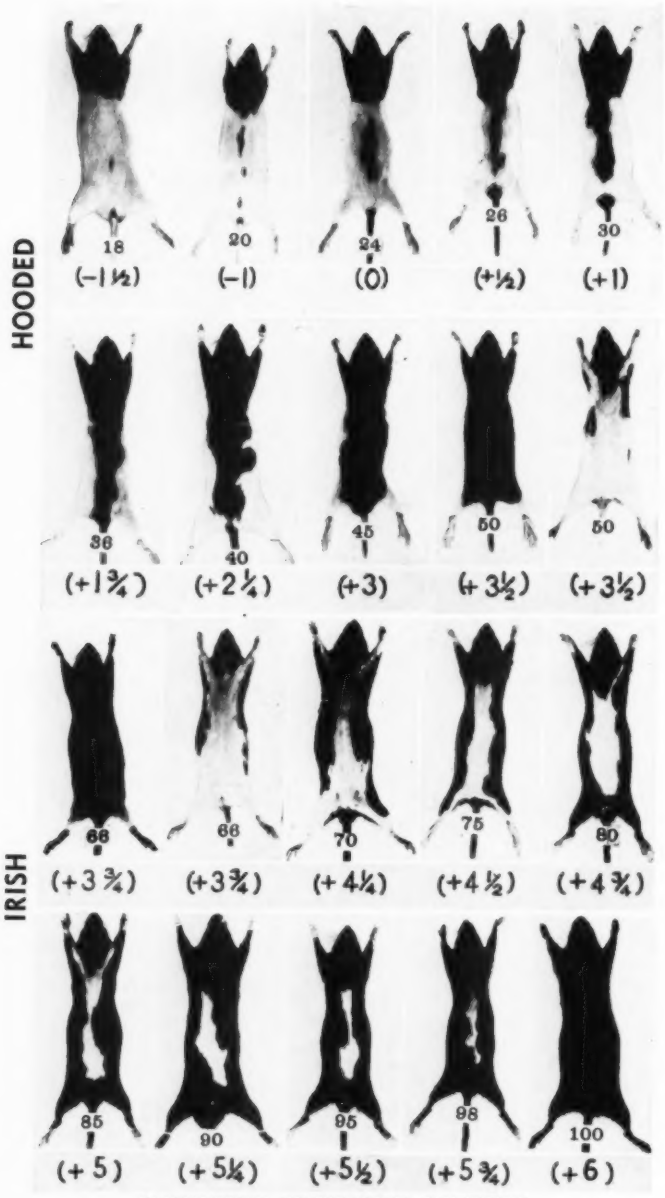
—But no mention of the gene.

MAN IN A CHEMICAL WORLD, The Service of Chemical Industry, *by* A. CRESSY MORRISON. American Chemical Society. Pp. 292. Price, $3.00. New York and London: Charles Scribner's Sons. 1937.

SEX LIFE IN MARRIAGE, *by* OLIVER M. BUTTERFIELD, Former Staff Member (Child Development and Parent Education) Teachers College, Columbia University. Pp. 192. Price, $2.00. New York: Emerson Books, Inc. 1937.

TWINS, A Study of Heredity and Environment, *by* HORATIO H. NEWMAN, FRANK N. FREEMAN, KARL J. HOLZINGER. Pp. 369. Price, $4.00. Chicago: University of Chicago Press. 1937.

TECHNOLOGY TRENDS AND NATIONAL POLICY, Including the Social Implications of New Inventions. Report of the Subcommittee on Technology to the National Resources Committee. Pp. 388. Price, $1.00 (Paper Cover). Washington, D. C.: Superintendent of Documents. June, 1937.



VARIATION OF HOODED PATTERN

Figure 3

The hooded pattern varies from eighteen per cent of the pelage black to a solid black coat, but the distribution of the pattern grades is not uniform, as is shown in Figure 4*A*. There it is seen that the hooded patterns (produced by the recessive gene *h*, fall into a clearly defined group having between 18 and 40 per cent of the coat pigmented. The Irish mutant (*h*) produces from 65 to 90 per cent pigmentation, and the dominant *H* gene solid colored (selfed) coats. This illustration shows eighteen steps (two of them duplicated [50 per cent and 66 per cent] to show both ventral and dorsal patterns) in the series from extreme white coat to extreme pigmented coat.

TWO INDEPENDENT MUTATIONS OF THE HOODED OR PIEBALD GENE OF THE RAT

And a Study of the Pattern Modifiers

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THE establishment of a pedigreed rat colony in 1920 at the Columbia University Institute of Cancer Research by Drs. Curtis and Bullock has been described in a previous publication.[1] These rats were from several independent strains each usually named for the breeder from whom the original stock was obtained and these strains were divided into inbred lines each of which arose from a single pair and was carried on by continuous brother by sister matings. The original stocks possessed in various combinations the following allelomorphic pairs of genes:

A, a: Agouti, non-agouti
C, c: Colored, albino
P, p: Black pigmented, yellow

but all of the colored animals and all of the albinos which were tested were genetically hooded (*h, h*). That is all of the animals which carried *C* had a colored head and stripe along the back. Some of the lines had a narrow stripe, others a medium or wide stripe. All of the lines showed some variation in the proportion of the coat which was colored but in one line this variation covered the entire range shown by the colony, varying from individuals with a colored head and one or two small spots on the back to individuals which were about one-half colored. No attempt had been made to select for pattern "modifiers" and the lines with relatively stable stripes resembled the original stocks from which they were derived.

Two independent mutations of the gene *h* (hooded) to its dominant allelomorph *h'* (Irish) have occurred in the inbred lines. These mutant individuals resembled the two mutants described by Castle and Phillips[2] which by subsequent testing were shown by them to be genetically identical and since these mutants had the same father they were believed to have been derived from a single mutation in the germ plasm of this sire. This mutation occurred in the plus selection series and these authors believed it improbable that such a mutation could have arisen in the minus selection series. The two mutations which occurred at the Columbia Institute for Cancer Research were in inbred lines derived from unrelated stocks and the two lines, both of which were relatively stable as to width of stripe, differed from each other in this respect.

On the Castle and Phillips scale, one line (20 to 30 per cent colored) graded approximately from —1 to +1 and the other (25 to 38 per cent colored) from +¼ to +2.

The first mutant born May 10th, 1924, was a fertile female about two-thirds colored (Castle and Phillips grade +3¾) and the mutant character was thoroughly tested and is established in a large number of her descendants. She is known to have the genetic constitution *AA, CC, pp, h' h.*

The second mutant, a black Irish male 84 per cent colored (Castle and Phillips grade +4¼), was born May 1, 1926, and was one of 37 progeny of a black hooded pair from the seventh brother × sister inbred generation of Zimmerman Line 898. With the exception of the mutant the animals of this family were all black hooded rats 28 to 38 per cent colored, having the genetic constitution *aa, CC, PP, hh.* Of the 36 sibs of the mutant 4 were older, 9 of the same litter, and 23 were younger. The mutant was

mated August 17, 1926, with his four litter-sisters and on January 15, 1927, he was also mated with an older sister which had just weaned her third litter by her litter brother. The animals all appeared to be in good physical condition when mature and they remained so for several months. All of the females were apparently healthy when the mutant died of pneumonia June 3, 1927. He was thirteen months of age and had been mated for nine and a half months but had not impregnated a female. His genetic constitution probably was *aa, CC, PP, h'h.*

The parents of the fertile mutant Irish female referred to above were of the third brother × sister inbred generation of the August Line 1561. They were both agouti pink-eyed yellow hooded rats heterozygous for agouti. The mutant had seventeen pink-eyed yellow hooded sibs four of which were non-agouti. Four of the hooded sibs were from the same litter as the mutant, six were older and seven were younger. The mutant and the litter brother with whom she was mated were both homozygous for agouti and of their 16 progeny, eight (4 males and 4 females) were Irish like the mutant and the other eight (7 males and 1 female) were hooded like their sire and other relatives. This is exactly the 1 : 1 ratio expected from the mating of a heterozygous Irish with a homozygous hooded individual indicating that this was a mutation of the *h* gene to the dominant *h'*. The percentage of the coat which was colored varied in the hooded animals of this family from 21 to 28 per cent while the mutant and each of her Irish offspring was 66 per cent colored (+3¾ grade of Castle and Phillips).

The daughters of the Irish mutant were distributed to their Irish brothers. One of the Irish males and one Irish female and the hooded female failed to produce offspring. The others produced 27 Irish and 6 hooded progeny. These Irish males were also mated with several hooded females and produced 104 progeny of which 78 were Irish and 62 hooded. The observed proportion of Irish and hooded individuals from these two types of matings differed from the appropriate Mendelian ratios within the range expected from fluctuations of sampling.

Observation on the 105 Irish grandchildren of the mutant showed that a few of the progeny of heterozygous Irish (*h' h*) pairs had a higher percentage of the coat colored than did their Irish parents or grandparent, and one of these mated with hooded females produced 10 Irish and no hooded progeny. It seemed possible that these were homozygous Irish individuals with less white than their relatives which were heterozygous for this character. Castle and Phillips[1] considered a similar explanation for the occurrence of offspring of their heterozygous mutants which graded higher than either parent. However Castle[3] later reported that the homozygous mutant race proved to be very stable in color varying only from +5¼ to +5¾ with a majoroity of animals graded as +5½ which was the grade of the narrower striped of the two original mutants.

Pattern Classification

Grading patterns in the descendants of the Irish mutant observed at the Columbia Institute for Cancer Research presented two difficulties which were obvious as early as the F_4 generation. First, in agouti yellow pink-eyed Irish individuals there was often an irregular band of hair colored like the stripe of a non-agouti hooded rat which merged into the white so gradually that it was difficult to be sure of the delineation of the pigmented area. This difficulty seemed to be accentuated when one of the parents was non-agouti. On the other hand the colored pattern was sharply defined in all black-eyed individuals. The second difficulty was in deciding the grade of the pattern since the scale published by Castle and Phillips although reasonably adequate for the hooded patterns seemed less satisfactory for the Irish patterns observed in this mutant series.

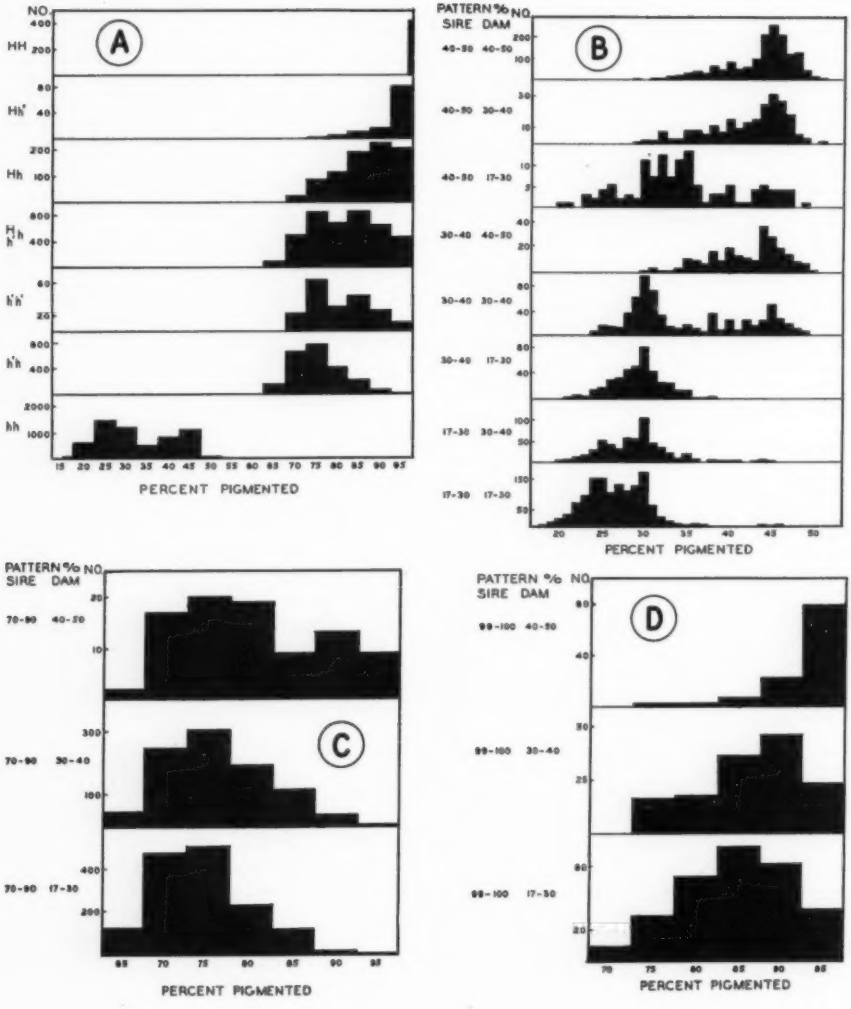
The first difficulty was evaded by classifying as Irish or hooded all animals in which the exact limit of the pattern was doubtful and not attempting to grade

them for use in analyses involving a quantitative study of the patterns. There was never any doubt as to which of the two groups an individual belonged. Since this difficulty of pattern extent was confined to pink-eyed individuals, black-eyed stocks were used almost exclusively in the testing experiments.

The second difficulty was partially overcome by constructing a chart from photographs of the animals of this mutant series itself supplemented by photograhs of hooded and also of heterozygous and homozygous selfed rats reared at this Institute after the occurrence of the mutation. The basis of this chart was the per cent of the coat which was colored. This had from the first seemed to be the logical scale and as a supplement to the grading by the Castle and Phillips' scale the per cent of area colored was estimated on the original mutant and her immediate descendants. In constructing the percentage chart however the measure of the total skin and of the colored area was obtained for a very small, a very large and for two hooded rats of intermediate sized and for small, medium and large Irish patterns. These measures were obtained by stretching the fresh skin on cross-section paper, outlining the margin, and pricking the outline of the patterns through the skins into the underlying cross-section paper. Then after removing the skins the outline of each skin and the punched pattern were traced as accurately as possible with a fine pen and the total area and the colored area obtained by counting the number of squares on the cross section paper and calculating the percentage of the total area which was colored. Then a large number of animals were killed and arranged in a series from the one with the smallest hood to a solid colored homozygous selfed individual. Each measured skin was matched to its nearest duplicate in this series and the percentage values were assigned as accurately as possible to the patterns between the ones which were matched to the measured skins. The assigned percentages were attached to the animals and from the series was selected for photographs a smaller series which included nearly every integral percentage from 18 to 50 (hooded) and every one from 65 to 100 (Irish or Selfed). The photographs were mounted on cards and rephotographed and reduced to a size convenient for making a working chart. Figure 3 shows about every fifth individual on the working chart with its percentage grade and in parentheses the grade assigned from the Castle and Phillips' chart.

Since the second Irish mutant at this Institute did not produce progeny it was not possible to test the identity of these two independent mutations or to test the second with its supposed allelomorphs. The first as shown by her immediate descendants was $h'h$ in which h' was dominant to h but whether or not this h' is identical with the similar mutation previously described by Castle and Phillips[2] is not known, since descendants from that mutation were not available for testing. However in 1925 a litter of 11 heterozygous selfed rats was presented to this Institute by Marcia Lakeland. They were the result of a spontaneous mating between her pet albino female and a wild Norway rat. Their progeny supplied abundant material for testing the mutant h' gene with H (self) to which it is recessive. Whether or not this mutation was identical with the one observed by Castle and Phillips it shares with it the characteristics of being the dominant allelomorph of hooded and the recessive of self.

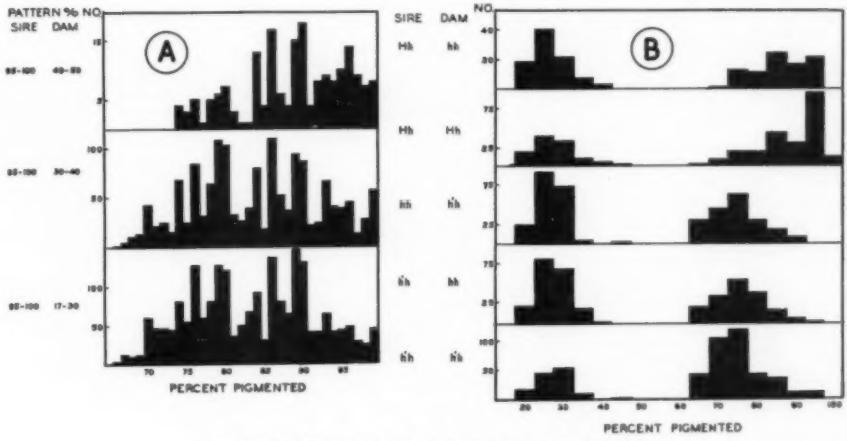
The fertile mutant had a considerably lower grade pattern than the sterile mutant and both were lower grade than the Irish mutants described by Castle and Phillips. In fact the fertile mutant and many of her heterozygous offspring overlapped in grade with the hooded rats in the "plus race" in which appeared the mutation reported by Castle and Phillips. The hooded members of her family were relatively narrow striped while the hooded relatives of the sterile mutant were of a grade between that of the family of the fertile mutant and the plus race of Castle and Phillips. It seemed probable that all three mutations were confined to a change of the gene h



DISTRIBUTION OF PATTERNS

Figure 4

A—Frequencies of pattern distribution of the various genotypes carrying the hooded gene and its allelomorphs. *B*—Distribution of pattern of homozygous hooded individuals grouped according to the pattern per cent of their parents. *C*—Influence modifiers shown by comparison of pattern per cent in progeny from the same sires by dams showing different extent of hooded pattern. *D*—Same for a group in which the sires were solid colored.



DISTRIBUTION IN F_1 AND F_2 MATINGS

Figure 5

A—Distribution of patterns of F_1 self males (*Hh'*), mated to females having three degrees of the hooded pattern. There is a significant difference in the distribution of the progeny in these three groups. *B*—Showing the pattern distribution in the progeny from the indicated matings, of various combinations of the hooded gene and its allelomorphs. The distribution is not what would be expected were more random assortment involved. A recessive lethal linked to the self (*H*) gene is believed to account for these differences.

to *h'* and that in each case pattern extension modifiers which affected either *h* or *h'* were inherited unchanged. Castle and Phillips were able to show this for their Irish mutation since crosses with the plus race from which it arose did not affect the grade or degree of variability of the Irish pattern but crosses with their "minus" race affected it permanently increasing its variability and lowering its grade even in the homozygous Irish individuals extracted from the cross.

In Table I and Figure 4*A* the frequencies for pattern per cent and the mean pattern per cent are given for the various genotypes. The patterns of 5,640 homozygous hooded individuals varied from 18 per cent colored to 60 per cent colored with the mean at approximately 35 per cent. The majority of hooded patterns fell between 20 per cent and 50 per cent colored. There were two exceptions at the upper end of the scale, one with a pattern of 55 per cent and the other 60 per cent colored. The frequency is bimodal with one mode at 45 per cent and the other at 30 per cent indicating the presence of modifying factors for the plus and the minus direction.

The other genotypes present an almost continuous range of variation from 66 per cent to 100 per cent colored with the means varying from 78 per cent for the 2,354 *h'h* progeny of homozygous Irish sires and hooded dams, through 83 per cent for the 196 homozygous Irish, 89 per cent for the 851 *Hh* selfed hooded heterozygotes, 96 per cent for the 108 *Hh'* or selfed Irish heterozygotes to 99.5 per cent for the 430 homozygous selfed individuals.

Two conspicuous gaps are obvious, that from 0 to 18 per cent colored and from 50 to 65 per cent colored. No colored individuals with less than the entire head being colored have been observed and no wide pattern hooded individuals with patterns indistinguishable from those of the heterozygous Irish (*h'h*) individuals were observed.

The patterns of the tested homozygous Irish individuals varied from 70 per cent to 98 per cent colored, and the frequency was also bimodal like that of the hooded individuals with one mode at 78 per cent and the other at 90 per cent,

Table I. Showing for Each Genotype the Frequency Distribution for the Per Cent of the Coat Which was Colored and the Mean ± P. E.

Group	Percent Pigmented																	Total	Mean ± P. E.
	10	20	30	40	50	60	70	80	85	90	95	100							
Hooded (hh)	20	548	1413	1705	514	282	1089	18	1	1								5640	54.0 ± .07
Irish + Hooded (h^{1}h)											149	685	780	448	225	65	15	2369	77.8 ± .08
Hooded x Irish (hh^1)											54	98	79	31	17			279	74.0 ± .22
Irish (h^{1}h^1)												22	64	30	48	26	11	196	80.8 ± .54
P$_1$ (Hh^1) x Hooded (Hh) or (h^{1}h)											90	409	688	695	665	649	467	4135	64.3 ± .09
Hooded x P$_1$(Hh^1) (Hh) or (Hh^1)											9	71	135	136	127	70	73	771	64.8 ± .22
Selfed x Hooded (Hh)												22	85	116	195	286	307	831	89.4 ± .16
Hooded x Selfed (Hh)											9	19	42	52	22	13		176	84.3 ± .53
Selfed x Irish (Hh^1)														1	9	8	14	80	196	96.8 ± .32
Selfed (HH)																	419	12	930	99.3 ±

Table III. Showing the Frequency Distribution and the Mean ± P. E. for the Pattern of the Heterozygous Irish Progeny according to the Pattern Grade of their Hooded Parents.

Pattern of Parent	Patterns of Progeny							
Sire	Dam	60	70	75	80	85	90	Total	Mean ± P. E.
70 - 90	17 - 30	125	496	388	251	113	14	1	1488	76.72 ± .09
"	30 - 40	42	240	306	197	116	30	5	939	78.56 ± .13
"	40 - 50	2	17	20	19	9	13	9	89	82.48 ± .60

Table IV. Showing the Frequency Distribution and the Mean ± P. E. for the Pattern of the Heterozygous Selfed Progeny according to the Pattern of their Hooded Parents.

Pattern of Parent	Patterns of Progeny						
Sire	Dam	70	75	80	85	90	Total	Mean ± P. E.
90 - 100	17 - 30	9	30	55	71	61	31	256	87.34 ± .28
"	30 - 40		17	10	37	47	24	140	89.07 ± .34
"	40 - 50		0	2	0	23	20	115	95.04 ± .28

Table II. Showing the Frequency Distribution and the Mean ± P. E. for the Pattern of the Hooded Progeny according to the Pattern Grade of their Parents.

| Pattern of Parent | | | Pattern of Progeny | | | | | | | | | | | | | | | | |

indicating that the color restricting or extending factors observed for the hooded pattern operate effectively in the presence of the Irish (h') allelomorph.

To test the allelomorphism of the mutant Irish (h') gene, crosses were made between the homozygous Irish and selfed individuals and the F_1 progeny were then backcrossed to hooded individuals. The patterns of 4,123 progeny from these F_1 sires and hooded dams and 571 progeny from the reciprocal cross varied continuously from 66 per cent colored to 99 per cent with the mean at 84 per cent. This distribution was bimodal with one mode at 79 per cent corresponding to the mean pattern of heterozygous Irish hooded ($h'h$) individuals and the other at 89 per cent corresponding to the mean pattern of heterozygous selfed hooded (Hh) individuals.

Figure 4*B* and Table II show the frequency for pattern per cent of the homozygous hooded individuals classified according to the pattern per cent of their parents. The patterns of the parents have been grouped into small (17 to 30 per cent), medium (30 to 40 per cent), and large (40 to 50 per cent) patterns. When both parents had small patterns, the patterns of the progeny showed an approximately normal distribution about a mean of 27 per cent. The progeny of small patterned sires with dams of intermediate pattern and of the reciprocal cross were also small patterned, the mean being 29.7 per cent. The progeny of two parents with patterns of from 40 to 50 per cent were wide patterned, the mean being 44 per cent. The progeny of wide patterned sires or dams with dams or sires of intermediate pattern were also wide patterned with a mean of 43 per cent. The distributions for the patterns of these wide striped progeny showed a sharp drop at about 50 per cent unlike the more or less normal distributions of the small patterned progeny. Whether this represents the limit of modification of the h gene or results from the lack of modifiers effecting the variation of the wide pattern or a deficiency in our scale of measurement at this point has not been determined.

The progeny of crosses between a wide and a narrow patterned parent were intermediate in pattern with a mean of 35 per cent. The progeny of two parents of intermediate pattern were of two types, small patterned and large patterned, indicating that two independent dominant modifiers of the h gene are involved. If half of the 94 progeny in the 30 per cent class from two parents with intermediate pattern are genetically small patterned as would be a fair assumption from their breeding histories, the 655 progeny from these parents might be classified as 250 with intermediate patterns, 196 with small patterns and 209 with wide patterns. Assuming that the narrow pattern results from a dominant pattern restricting gene (R) and that the wide pattern results from the presence of a pattern extending gene (W) and that the hybrids and double recessives would be intermediate in pattern it is a fair 6 : 5 : 5 ratio, the expected being 246 intermediate, and 205 each of wide and small patterns.

The influence of these modifiers of the hooded pattern on the Irish (h') allelomorph may be seen from Table III and Figure 4*C*. The 1568 progeny of an Irish parent and a hooded parent of small pattern had a mean pattern of $76.72 \pm .09\%$ while the mean pattern of 959 progeny from the same Irish parents and hooded parents of intermediate pattern was significantly larger or $78.56 \pm .13\%$. When the hooded parent had a wide pattern, the mean pattern per cent of the progeny was $82.48 \pm .60$, or significantly larger than that of a smaller patterned parent.

In the next table (IV) and Figure 4*D* similar data on a smaller group of self $\times$ hooded hybrids are given. When the hooded parent had a small pattern the mean pattern per cent of the progeny was $87.52 \pm .28$. Hooded parents of intermediate pattern (Hh) had selfed hooded hybrid progeny with a significantly higher pattern the mean being $89.07 \pm .34\%$. From the wide striped hooded parents the patterns of the progeny were significantly larger than from either of the other groups the mean be-

ing 95.64±.28%. Thus the dominant modifiers of the hooded pattern are seen to similarly modify the Irish (*h'*) and self (*H*) allelomorph.

The next Table (V) and Figure 5*A* show the pattern percentage of the progeny of F_1 (*Hh'*) males with hooded females of small, medium and large patterns. The mean pattern varied significantly in the three groups being the largest for the progeny of the wide patterned parents. The patterns of the females in Table V appear to be slightly smaller than of the males of the same group. Possibly due allowance was not made for the slight difference in size between the animals of the two sexes when the patterns were taken. These distributions have the characteristic bimodal form, the one mode representing the average pattern for the Irish hooded (*h'h*) heterozygote and the other the average pattern of the selfed hooded (*Hh*) heterozygotes.

Table VI and Figure 5*B* show the ratio of hooded to Irish and selfed progeny from two heterozygotes and from the heterozygous individuals backcrossed to hooded individuals. In the first group, heterozygous selfed hooded sires and hooded females had 87 hooded and 86 heterozygous selfed progeny of average pattern. When both parents were heterozygous selfed the progeny were 102 hooded and 218 selfed and heterozygous selfed. This latter group should have been approximately 300 for the expected 3:1 ratio. Since the same sires with hooded females showed no deficiency among the heterozygous selfed progeny, it seems likely that this deficiency is in the expected homozygous selfed progeny. The nine 100% colored progeny were homozygous selfed and of the 95 with patterns from 95 to 100%, 23 were known to be heterozygous and 7 with 99% pattern were known to be homozygous selfed and 65 were untested. If the latter were heterozygous or mostly heterozygous this group approximately equaled the expectation. Only 16 were known to be homozygous whereas approximately 100 were expected. It seems likely that a recessive lethal linked with the selfed or (*H*) gene was picked up from the wild ancestor. It was with considerable difficulty that the homozygous selfed stock was established and in several instances the homozygous selfed males bred only with their known heterozygous sisters or with out-crossed hooded females.

The progeny of two heterozygous Irish parents were 125 hooded and 364 Irish individuals of average pattern or approximately a 3:1 ratio of Irish to hooded progeny.

Summary

1. Two dominant mutations from the hooded to the Irish pattern were observed.
2. One mutant was a fertile female and was heterozygous for the Irish or mutant gene.
3. This mutant gene (*h'*) proved to be the dominant allelomorph of hooded (*h*) and to be recessive in its expression to the self pattern.
4. Independent dominant pattern extending and restricting factors modified the hooded pattern and functioned similarly in the presence of the mutant (*h'*) Irish and self (*H*) allelomorphs.
5. A recessive lethal was observed which was linked with the (*H*) gene picked up from a wild ancestor.

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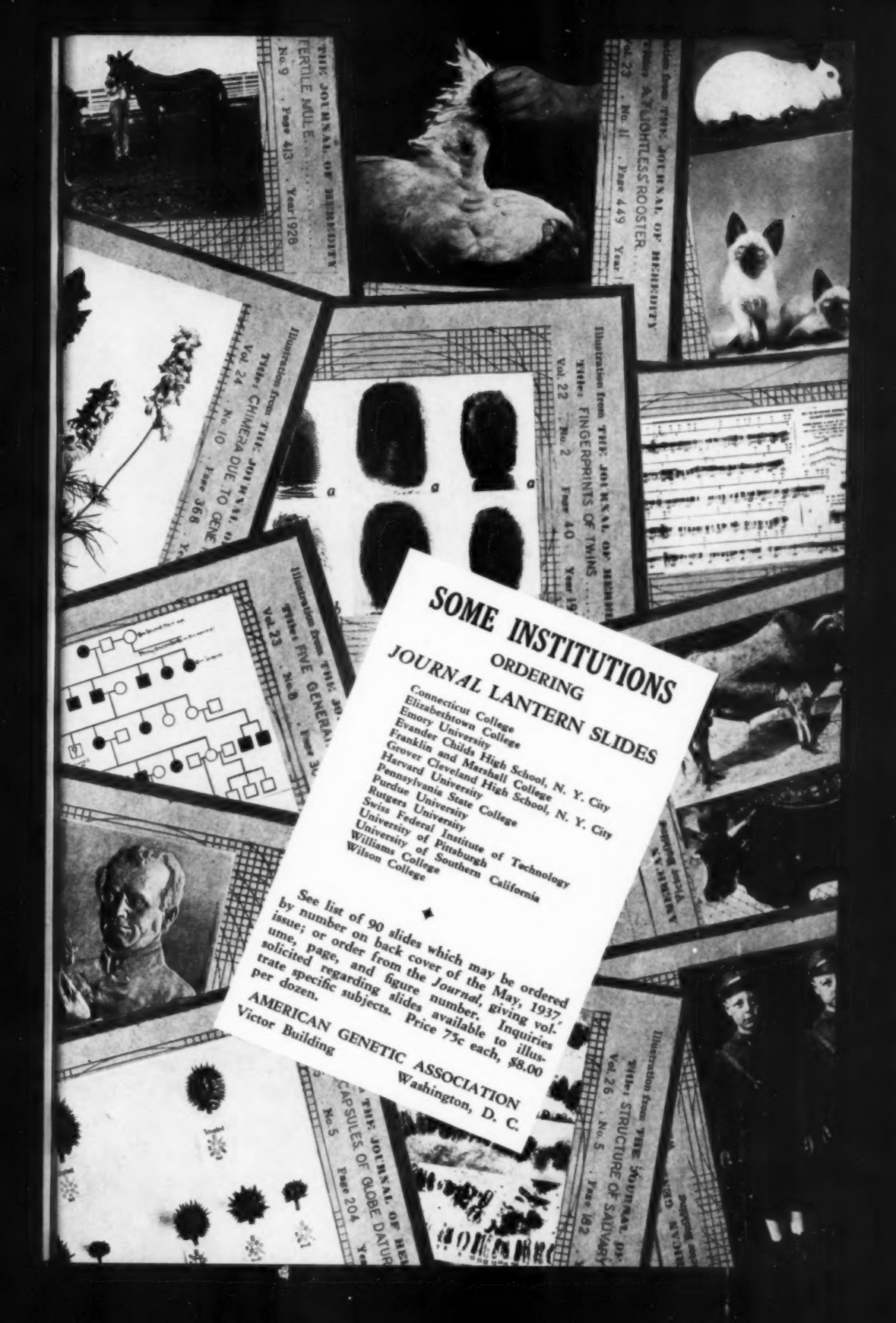
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